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Editorial Comment

Can Electrophysiologic Testing Predict Mortality After Myocardial Infarction?*

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In patients discharged from the hospital after an acute myocardial infarction, a number of factors, including degree of left ventricular systolic dysfunction (1) and the presence of complex ventricular ectopic activity (2), have been shown to be markers for increased cardiovascular and sudden death. However, the overall value of these factors in predicting sudden cardiac death is only in the 30% range. Because of the strong correlation between clinical occurrences of sustained ventricular tachycardia and the ability to induce monomorphic ventricular tachycardia in the laboratory (3), programmed ventricular stimulation has recently been applied to patients after myocardial infarction in an effort to improve the predictive accuracy for identifying those at high risk for sudden cardiac death. The results to date have been controversial.

Summary of findings in postinfarction programmed ventricular stimulation studies. The six studies (4–9) that have addressed the role of programmed ventricular stimulation in identifying high risk patients after myocardial infarction have followed the same general outline. A selected population of patients with acute myocardial infarction was subjected to programmed ventricular stimulation from 6 to 60 days after admission, with a stimulation protocol that included double and in one case triple ventricular extrastimuli of twice diastolic threshold to 20 mA in amplitude. In each study ventricular electrical instability was defined as the induction of nonsustained ventricular tachycardia (>4 complexes to >10 seconds) or sustained ventricular tachycardia or ventricular fibrillation. The patients were followed up prospectively for a mean of 8 to 23 months, with the end point being sudden cardiac death or spontaneous ventricular tachycardia or ventricular fibrillation.

In these studies, ventricular tachyarrhythmias were inducible in a significant percentage of the patients (17 to 46%), and were equally distributed between nonsustained and sustained ventricular tachycardia. Using this approach, three studies found a significant correlation between ventricular electrical instability and subsequent sudden cardiac death or ventricular tachycardia (4–6), whereas three failed to find such a correlation (7–9).

Reasons for differences in the outcome of the studies. Several factors may account for these differences in outcome, including differences in the stimulation protocol (10,11), timing of performance of programmed ventricular stimulation relative to the infarction and the subsequent use of beta-blocker or antiarrhythmic therapy during follow-up (12). The three most important factors that might influence the outcome of the studies and may account for the major discrepancies are the demographics and size of the study population and the duration of follow-up. All three factors are critical because they profoundly influence the mortality rates in the study population.

To obtain a statistically meaningful result, a minimal difference in mortality rates must be achieved between the two groups being compared (13). To generate the necessary number of deaths, a large enough population would have to be enrolled based on the expected mortality rates for patients discharged after an infarction. Furthermore, exclusion criteria should not be overly restrictive or they may markedly alter the risk profile of the study group and reduce mortality rates. This will also directly reduce the specificity of a given marker for sudden coronary death mortality (14) by reducing the pretest probability of its occurrence. Finally, an appropriate follow-up period, which should be judged by the minimal and not the mean duration of follow-up, should be employed; otherwise, the mortality rate could be artificially reduced, by not allowing an observation period long enough for the expected deaths to occur. Thus, a study incorporating a population that is too small or shorn of its higher risk subpopulation, or both, and which has been followed up for too short a time, will yield too few deaths to allow a statistically meaningful result to be obtained.

Unfortunately, all but two of the studies cited involve these major methodologic flaws. Only those of Richards et al. (5) and Waspe et al. (6) have a large enough number of deaths to allow a meaningful conclusion to be drawn about the correlation between postinfarction ventricular electrical stability on the one hand and sudden cardiac death and ventricular tachycardia on the other.

Implications for the present study. The results of the study of Kersschot et al. (15), reported in this issue of the journal, are difficult to generalize. The small study population, which is subdivided into two groups for comparison of the influence of reperfusion on inducibility of ventricular

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tachycardia, and the restrictive exclusion criteria produce too few deaths to allow a meaningful evaluation of the correlation between ventricular electrical stability and sudden cardiac death or spontaneous ventricular tachycardia.

Furthermore, the results show a much better than expected effect of reperfusion with streptokinase on preservation of left ventricular systolic function than has been previously reported (16), and the rate of inducibility of ventricular tachyarrhythmias (100% in the nonreperfused group) is much higher than in any of the previously reported studies (4–9).

The only conclusions that might be drawn from the present study are that successful early reperfusion of the myocardium in the course of an acute myocardial infarction may be associated with 1) a lesser degree of residual myocardial damage, and 2) a lower inducibility rate for ventricular tachyarrhythmias by programmed ventricular stimulation. The clinical implication of the latter finding is not clear.

Conclusions. The controversy over the predictive value of programmed ventricular stimulation for identifying patients at high risk soon after acute myocardial infarction is currently unresolved. Resolution of the controversy will depend on the results of new studies that obviate the previous methodologic flaws. What is needed are studies incorporating larger populations, in which high risk patients are not excluded and reasonably aggressive stimulation protocols (higher stimulation energy levels or triple extrastimuli, or both) are applied. In addition, the minimal follow-up duration should exceed 18 months, and to whatever degree possible, empiric antiarrhythmic drug therapy should be restricted during the follow-up period. Once the results of such studies are available, the impact of various interventions, including antiarrhythmic drug therapy, bypass surgery or early reperfusion, on the relation between postinfarction ventricular electrical instability and identification of high risk patients, can be meaningfully evaluated.

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